REMARKS

Status of Claims:

Claims 12 and 14-25 were pending in the application. Claim 25 is hereby cancelled without prejudice to, or disclaimer of, the subject matter contained within. Claims 12 and 14-24 are now pending. Each claim defines an invention that is novel and unobvious over the cited art. Favorable consideration of this case is respectfully requested.

Rejections Under 35 U.S.C. § 112, 2nd Paragraph:

Claims 12 and14-25 were rejected under 35 U.S.C. § 112, 2nd Paragraph, as being indefinite.

Claim 12 is hereby amended to recite "basophil" and "hemoglobin" as suggested by the Examiner.

Claim 25 is hereby cancelled without prejudice or disclaimer of subject matter contained within.

Rejections Under 35 U.S.C. § 112, 1st Paragraph:

Claim 25 was rejected under 35 U.S.C. § 112, 1st Paragraph, as containing subject matter which was not described in the specifications is such a way as to reasonably convey to one skilled in the relevant are that the inventor, at the time the application was filed, had possession of the claimed invention.

Claim 25 is hereby cancelled without admission or any prejudice to, or disclaimer of, the subject matter contained within.

Rejection Under 35 U.S.C. § 103(a):

Claims 12 and 14-25 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Sakata (5,538,893) in view of Hamaguchi et al. (5,389,549) and further in view of Uchihashi (5,968,832).

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka.* All words in a claim must be considered in judging the patentability of that claim against the prior art. *In re*

Wilson. (MPEP § 2143.03). When evaluating the scope of a claim, every limitation in the claim must be considered. See e.g. *In re Ochiai.* (MPEP § 2144.08). The evidentiary record fails to teach each limitation of the present invention.

The present invention, as recited in amended claim 12, comprises a single-solution, cyanogen-free reagent that permits: (1) the counting of total leucocytes, (2) the counting of basophils, and (3) the determination of total hemoglobin in a sample of blood. Moreover, the single reagent comprises a nitrogenous compound, preferably a thiourea, at least one cationic detergent, and a buffer that maintains the pH at an acidic value less than 3. Preferably, the buffer maintains a pH of 2.4.

As disclosed in the original specification (page 2, 1st and 2nd paragraphs), the numeration of basophils is particularly tricky. In a normal, healthy human, basophils comprise only about 0.5 to 1% of total leucocytes. Various conditions of medical concern, such as infections, allergic reactions, and metabolic diseases can cause an increase in the proportion of basophils, but only up to 2 to 3% by weight of total leucocytes.

The Examiner acknowledges that Sakata and Hamaguchi fail to teach determination of hemoglobin. (Paper 5, page 7). Sakata and Hamaguchi each further fails to teach a nitrogenous compound such as a thiourea. The nitrogenous compound, which is preferably thiourea, functions to stabilize the by-products of hemoglobin oxidation. Because Sakata does not teach the determination of hemoglobin, that reference is understandably silent. Hamaguchi teaches a dual reagent. Hamaguchi teaches away from the single reagent of the present invention. Furthermore, Hamaguchi is not properly combinable with Sakata. Hamaguchi teaches a two-step method to differentiate the various leucocyte populations. Each step requires different assay conditions, and therefore, a different reagent. The art cited by the Examiner, does not provide a reasonable expectation of success because Hamaguchi teaches that the differentiation of various leucocytes populations requires separate assay conditions.

Moreover, Sakata teaches away from the present invention. Sakata requires the pH to be in the range from 2.5 to 4.0 and preferably from 3.0 to 4.0 (Column 5, lines 25-27). Whereas, according to preferred aspects of the present invention, the pH is 2.4 (claim 14). Sakata states that such a low pH is to be avoided because a pH below 2.5

causes the nuclei of immature granulocytes to become bared. (Column 5, lines 27-29). Teaching away from the invention is a *per se* demonstration of nonobviousness. U.S. v. Adams, 338 U.S.39, 148 U.S.P.Q. 479 (1966).

The Examiner suggests that Uchihashi completes the teaching of Sakata by teaching the determination of hemoglobin. However, Uchihashi is not able to measure basophils. Rather, Uchihashi measures lymphocytes in a first embodiment and lymphocytes and neutrophils in a second embodiment. Uchihashi is not properly combinable for the instant purpose because Uchihashi forms inoperable combinations. First, Uchihashi recites "[t]he buffer is not restricted as long as it can maintain a pH at 4.0 to 6.0. Too low a pH makes leucocytes fragile, thereby adversely affecting the measurement of the leucocyte count." (col. 3, lines 49-51). The present invention requires the buffer to maintain a pH value lower than 3. In addition, Uchihashi cannot be combined with other art to yield the present invention because hemoglobin is unstable at the higher pH used by Uchihashi. The art faces a dilemma: at too high a pH, hemoglobin is unstable, but, at the lower pH where hemoglobin is stable, leucocytes are unstable. The reagent of the present invention resolves this dichotomy and permits determination of hemoglobin and counting of basophils.

Secondly, The Examiner's combination of Uchihashi with Hamaguchi is improper because Uchihashi and Hamaguchi form an inoperable combination. Hamaguchi recites solutions that do not "employ either saponin or quaternary ammonium compounds." (Abstract). Moreover, Hamaguchi considers "quaternary ammonium salts cause an undesirably high degree of damage to leucocytes." (Col. 5, lines 61-63). Hamaguchi specifically excludes quaternary amines "whereas quaternary ammonium salts are too violent as noted above...neither saponin or quaternary ammonium salts are used." (Col 6, lines 34-48). Uchihashi specifically recites quaternary amines "The cationic surfactant preferably includes at least one cationic surfactant of the quaternary ammonium salt type or pyridinium salt type." (Col. 2, lines 49-51; col. 4, ex. 1-3).

Where the Examiner proposes a combination that makes a prior art reference inoperable for its intended purpose, the resulting inoperable prior art reference is considered to teach away from the proposed combination, thereby supporting a showing of nonobviousness. *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984) (Finding no

suggestion to modify a prior art device where the modification would make the device inoperable for its intended purpose); *TecAir, Inc. v. Denso Mfg. Michigan Inc.*, 192 F.3d 1353, 52 USPQ 2d 1294, 1298 (Fed. Cir. 1999) (Holding that because the combination was inoperable for its intended purpose, a jury could reasonably find the patent taught away from the combination); *In re Sponnoble*, 405 F.2d 578, 587 (CCPA 1969)(Holding if where combined, the references would produce a seemingly inoperative device, the references teach away from their combination).

Conclusion:

In view of the above, consideration and allowance are, therefore, respectfully solicited.

In the event the Examiner believes an interview might serve to advance the prosecution of this application in any way, the undersigned attorney is available at the telephone number noted below.

The Commissioner is hereby authorized to charge any fees or credit any overpayment associated with this communication, including any extension fees or fees for the net addition of claims, to Deposit Account No. 22-0185.

Respectfully submitted,

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